Lgr5-mediated self-renewal in B cell selection and leukemia-initiation

Grant Award Details

Lgr5-mediated self-renewal in B cell selection and leukemia-initiation

Grant Type: Quest - Discovery Stage Research Projects

Grant Number: DISC2-10061

Project Objective: Lgr5-mediated self-renewal in B cell selection and leukemia-initiation

Investigator:

Name:	Markus Müschen
Institution:	City of Hope, Beckman Research Institute
Type:	PI

Disease Focus: B cell cancers, Blood Cancer

Human Stem Cell Use: Cancer Stem Cell

Award Value: $2,186,520

Status: Active

Grant Application Details

Application Title: Lgr5-mediated self-renewal in B cell selection and leukemia-initiation

Public Abstract:

Research Objective

LGR5-antibody drug conjugate to target LIC in B cell tumors that undergo self-renewal

Impact

LIC were only defined in myeloid leukemia, while LIC populations in B cell tumors remain elusive. LICs give rise to drug-resistance and relapse and remain unsolved clinical problems in B cell tumors.

Major Proposed Activities

- Proof of concept studies- Positive selection by antigen-receptor (BCR) signals drives self-renewal in normal B cell development and leukemia and lymphoma.
- Define patient groups and B cell leukemia and lymphoma subtypes that will benefit from LGR5-ADC mediated eradication of LIC.
- Safety and efficacy profiles - choice of LGR5-ADC based on safety and efficacy profiles in quiescent Lgr5+ populations
- In vivo testing platform –optimizing LGR5-ADC efficacy and therapeutic window
- IND-enabling studies, concept for multicenter phase 1 clinical trial to test safety and tolerability of LGR5-ADC in patients woth pre-B ALL and mature B cell lymphoma.

Statement of Benefit to California:

B cell tumors account for an estimated ~129,000 newly diagnosed patients in 2015 in the US and California. Despite improvements, survival rates recently leveled off near 60%. 40,000 patients are expected to die from B cell tumors in the US and California this year. 1.2 million people are currently living with or recovering from B cell tumors. Therefore, stem cell-based efforts to reduce toxicity and minimize late effects are an important aspect in the development of new therapy strategies.
